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Terms	Documents
sparg$ same (liposome or vesicle)	17

Database:
US Pre-Grant Publication Full-Text Database
US Patents Full-Text Database
US OCR Full-Text Database
EPO Abstracts Database
JPO Abstracts Database
Derwent World Patents Index
IBM Technical Disclosure Bulletins

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Search History

DATE: Monday, August 07, 2006 Printable Copy Create Case

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DB=USPT,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=OR			
L1	sparg$ same (liposome or vesicle)	17	L1

END OF SEARCH HISTORY

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L1: Entry 13 of 17 File: USPT Mar 3, 1998

DOCUMENT-IDENTIFIER: US 5723147 A
** See image for Certificate of Correction **
TITLE: Multivesicular liposomes having a biologically active substance encapsulated therein in the presence of a hydrochloride

Detailed Description Text (15):
The volatile organic solvent is removed, for instance by evaporation, from the spherules. When the solvent is completely evaporated, multivesicular liposomes are formed. Representative gases satisfactory for use in evaporating the solvent include nitrogen, helium, argon, oxygen, hydrogen and carbon dioxide. Alternatively, the organic solvent can be removed by sparging, rotary evaporation, or solvent selective membranes.

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L1: Entry 16 of 17 File: USPT Jul 30, 1996

DOCUMENT-IDENTIFIER: US 5540936 A
TITLE: Method of producing liposomes

Brief Summary Text (5):
In one method for the manufacture of liposomes, the organic and aqueous phases are combined in a reactor, typically equipped with a mixing assembly. The combined phases are mixed together under heating while the organic solvent is removed. This is typically accomplished by bubbling an inert gas (e.g. nitrogen gas) through the mixture, a procedure often referred to as sparging.

Brief Summary Text (22):
This aspect of the present invention is premised on the discovery that three of the many variables in the described process for producing liposomes are highly influential in determining the size distribution of the liposomes produced by that process. These three principal variables are 1) the relative speed of the mixing apparatus; 2) the rate of flow of the inert gas to remove the solvent from the mixture of the organic and aqueous phases (that is, the sparge rate); and 3) the temperature of the mixture (that is, the reaction temperature). The present inventors have determined that there is a relationship between these three variables such that, by an appropriate selection of the variables, a liposome population having a single-modal population distribution encompassing a preselected mean particle size can be obtained.

Brief Summary Text (23):
The size distribution of the liposomes is generally affected by these three principal variables in the following manner. As the mixing speed or the temperature of the reaction is increased, the size of the liposomes will generally decrease. Conversely, as the sparge rate is increased, the size of the liposomes will generally increase. Accordingly, the process of the present invention for the production of liposomes in its broadest aspect comprises selecting a desired mean liposome size, combining an organic phase, composed of an amphipathic lipid in a water-immiscible solvent, with an aqueous phase which optionally may include a bioactive agent, and mixing the combined phases at a preselected mixing speed, sparge rate and reaction temperature in accordance with the desired mean particle size of the liposomes. In particular embodiments, the solvent to aqueous phase volume ratio of the components is less than 3:1, and the process is conducted at a pH in the range most compatible with the lipid material, typically 5.5 to 7.5.

Brief Summary Text (25):
The combined organic solvent and aqueous phases are processed in a reaction vessel under process conditions, including mixing speed, inert gas flow rate and reaction temperature sufficient to produce liposomes. The preselected mixing speed, sparge rate and reaction temperature may be chosen in accordance with the following equation:

Detailed Description Text (2):
In accordance with the present invention, a multilamellar liposome is formed based on a preselected mean particle size using less solvent and more favorable pH conditions than in prior methods. The process of this invention involves combining an organic phase and an aqueous phase, in a ratio of organic phase to aqueous phase

(volume/volume) of less than about 3:1, and preferably with a volume ratio of less than about 1:1, so as to form a biphasic mixture. It is desirable that the least amount of organic solvent be used, to facilitate its removal. However, a minimum volume ratio of about 0.13:1 was found to be needed to achieve adequate drug entrapment, with a minimum ratio of 0.20:1 being preferred. In general, the minimum amount of organic solvent is used which can produce the desired liposome product. As a result of using less solvent than previously described methods, the overall volume of inert gas employed and the length of time of the sparging operation may be reduced.

Detailed Description Text (10):
Prior to conducting the liposome-forming process, a desired mean particle size is selected, typically depending on what agent is to be incorporated in the liposome or on the end use of the liposome. For example, when gentamicin is incorporated into the liposome, a typical mean particle size is about 200 nm. The components necessary to form the liposomes or the viscous gel intermediate are combined in the following manner. An amphipathic lipid or mixture of lipids is dissolved in a water-immiscible organic solvent to form an organic phase. After selecting the desired mean particle size, the organic phase is added to the aqueous phase. The mixture is then processed, typically in a reaction vessel, for example, a reaction vessel of the type, for example, shown in FIG. 1. Referring to FIG. 1, there is shown a processing system 2 including a vessel 4 defining a processing space 6 wherein the organic and aqueous phases are mixed together in accordance with the invention. The vessel is provided with a mixing system 8, a sparge system 10 and a heating/cooling system 12.

Detailed Description Text (73):
As shown by a review of the data in Table 2, varying the mixing speed, inert gas flow rate (sparge rate) and/or reaction temperature will affect the mean particle size of the liposomes. A comparison of Examples 1 and 2 shows that, by increasing the mixing speed (from 1,000 to 2,000 rpm), while holding the sparge rate and reaction temperature constant, there is a decrease in the mean particle size. A comparison of Examples 1 and 3 shows that an increase in the sparge rate (from 0.04 to 0.8 L/min), while holding the mixing speed and reaction temperature constant, results in an increase in the size of the liposomes. If just the reaction temperature is increased (compare Examples 1 and 5), the size of the liposomes generally decreases.

Detailed Description Text (88):
The heated reaction mixture was then sparged with nitrogen gas at the rate of about 1.0 L/min. In less than two minutes a viscous gel was formed having an appearance, when viewed under a microscope, similar to that shown in the FIG. 3 micrograph. The process was continued until the methylene chloride content was reduced to a level of no more than 0.1% by volume and liposomes formed.

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Search Results -

Terms	Documents
L4 and 424/$.ccls.	16

Database: US Pre-Grant Publication Full-Text Database; US Patents Full-Text Database; US OCR Full-Text Database; EPO Abstracts Database; JPO Abstracts Database; Derwent World Patents Index; IBM Technical Disclosure Bulletins

Search: L5

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Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=OR			
L5	L4 and 424/$.ccls.	16	L5
L4	(impeller adj1 mixer)	391	L4
L3	vesicle and (impeller adj1 mixer)	0	L3
L2	liposome and (impeller adj1 mixer)	6	L2
L1	liposome same (impeller adj1 mixer)	0	L1

END OF SEARCH HISTORY

L5: Entry 13 of 16 File: USPT Sep 21, 1999

DOCUMENT-IDENTIFIER: US 5955143 A
TITLE: Hollow polymer microcapsules and method of producing the same

Brief Summary Text (32):
The finely divided particles of solid core material are dispersed into the polymer solution which, as described above, is a volatile nonaqueous solvent that contains the solubilized polymer. The polymer solution containing the dispersion or suspension of particulate solid core material is prepared by conventional mixing methods, and mixing techniques that involve high shear mixing are preferred. Such high speed mixers may include Waring.RTM. blenders (for laboratory scale use), high shear mixers, e.g., rotating impeller mixers or in-line mixers, homogenizers, and the like. Grinding, milling or comminution devices that provide high shear during their operation may also be used to form the dispersion of particulate solid core material in the polymer solution, since such equipment is especially useful for concurrent particle size reduction and dispersion of the finely divided particles into the polymer solution.

Current US Cross Reference Classification (1):
424/489

Current US Cross Reference Classification (2):
424/490

Current US Cross Reference Classification (3):
424/493

Current US Cross Reference Classification (4):
424/497

Current US Cross Reference Classification (5):
424/501

Current US Cross Reference Classification (6):
424/9.52

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L5: Entry 15 of 16 File: USPT Nov 29, 1988

DOCUMENT-IDENTIFIER: US 4788001 A
TITLE: Oil-in-water emulsion

Brief Summary Text (60):
Any mixing means can be used in the process of this invention provided only that it is capable of intimately mixing the components of the emulsion to be prepared. Examples of suitable mixing means include, but are not limited to, impeller mixers, sigma blade dough mixers and planetary mixers.

Current US Cross Reference Classification (3):
424/65

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Search Results -

Terms	Documents
(liposome) same (static adj1 mixer)	10

Database: US Pre-Grant Publication Full-Text Database; US Patents Full-Text Database; US OCR Full-Text Database; EPO Abstracts Database; JPO Abstracts Database; Derwent World Patents Index; IBM Technical Disclosure Bulletins

Search: L2

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Search History

DATE: Monday, August 07, 2006 Printable Copy Create Case

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DB=USPT,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=OR			
L2	(liposome) same (static adj1 mixer)	10	L2
L1	(multivesicular) same (static adj1 mixer)	1	L1

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L2: Entry 7 of 10 File: USPT Nov 1, 1988

DOCUMENT-IDENTIFIER: US 4781871 A
TITLE: High-concentration liposome processing method

Detailed Description Text (55):
During the second, solvent-injection phase of operation, liposomes are produced as the lipid solvent is removed from the lipid-in-solvent/buffer mixture. Here the lipid-in-solvent solution in tank 62 is introduced into chamber 66 by the metering pump 68, and aqueous buffer held in tank 64 is fed into the mixing chamber under pressure. The two solution mix in mixing chamber 66 and the lipid-in-solvent/buffer mixture is subsequently mixed with the aqueous buffer being recirculated through the solvent removal subsystem immediately upstream of static mixer. Importantly, at the point of mixing, all solutions are at a temperature below the boiling point of the lipid solvent. As the mixture passes through the static mixer the temperature is raised to a point above the boiling point of the lipid solvent (at the pressure set in the vacuum chamber). Following passage through the static mixer, the mixture is sprayed into the vacuum chamber as a fine mist by nozzle 75. Since the lipid solvent will vaporize at the temperature and pressure present in the chamber, the bulk of the solvent is stripped from the mixture as the droplets fall through the chamber. The vaporized solvent is condensed by a condenser (not shown) connected to the vacuum system. The lipid which is left behind as the solvent is removed, forming liposomes ranging in size between about 0.1 to 20 microns in diameter. The lipid-in-solvent/buffer mixture injection coupled with solvent removal continues until the lipid concentration in the aqueous phase reaches the desired level, whereupon valve 80 is adjusted to divert a fraction of the fluid supplied from pump 78 to the down-sizing filter subsystem. A balance is struck so that the same volume of buffer entering through the injection system is diverted to the down-sizing filter subsystem.

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L2: Entry 6 of 10 File: USPT Aug 19, 1997

DOCUMENT-IDENTIFIER: US 5658898 A
TITLE: Intravenous solutions for a derivative of staurosporine

Brief Summary Text (66):
The aqueous liposome dispersion comprising the phospholipid component b) of formula I is prepared by using a process for the preparation of liposomes which is known per se, for example by homogenising a coarse aqueous dispersion comprising the phospholipid component b) by intensive shaking using a dispersing apparatus, for example a Vortex mixer, static mixers or dispersing apparatus of the POLYTRON type (Kinematica AG, Littau CH) or dispersing apparatus from EKA (DE-Staufen). By such means liposomes are formed that may be large, small, unilamellar or multilamellar. Approximately from 0.1 to 50.0% by weight, based on the total weight of the aqueous dispersion in that preliminary stage of the process, preferably approximately from 2.0 to 20.0 % by weight, are dispersed in the aqueous phase. During the preparation of the liposome dispersion, the so-called phase-transition temperature (gel-like/liquid crystalline) of the phospholipids used is critical. The dispersion is carded out preferably at temperatures at which the phospholipids are in the liquid crystalline state, (hat is to say above the so-called phase-transition temperature. Phospholipids that are in the liquid crystalline state at room temperature or lower temperatures are especially suitable. The liposomes are, where appropriate, prepared at temperatures below room temperature and/or under an inert gas atmosphere.

L2: Entry 5 of 10 File: USPT Dec 23, 1997

DOCUMENT-IDENTIFIER: US 5700482 A
TITLE: Process for the preparation of a liposome dispersion under elevated pressure contents

Detailed Description Text (2):
The pumps 2 and 7 convey the CO.sub.2 and the modifier from the reservoirs 1 and 6 into the apparatus. The CO.sub.2 pump is preferably cooled to -10.degree. C., the CO.sub.2 having a density of approximately 1 g/ml and being easy to pump. The pump pressure safety device 3 displays the pressure of the pumps 2 and 7. The pulse damper 4 damps the pressure pulses of the pumps 2 and 7, which occur when the pump piston is retracted. The pump control 8 controls the flow and the phase mixing ratio of the two pumps 2 and 7. The static mixers 9, 20, 25, 33 have no movable parts. Mixing occurs as a result of currents in a steel tube in which several mixing elements (current breakers) are incorporated, which splits and collects the current lines. The dynamic mixer 10 has a movable part. The movement produces a turbulent current, which mixes the phases introduced. The filter 11 retains undesired foreign particles in the mobile carrier phase consisting of CO.sub.2 and modifier. The injector 12 is provided for further additions of modifier. The check valve 13 allows the mobile carrier phase to pass only in the direction A.fwdarw.B. Should the pressure in direction B fall and become less than the pressure in direction A, compressed phase is introduced until stable, equal pressure conditions prevail. The adjustable pressure safety valve 14 opens in the case of undesired overpressure. The cross piece 15 is open in all directions. The manometer 16 displays the pressure in the recycling circuit I, which is defined by the arrangement C-D-19-20-F-G-18-17-15-C, or, preferably, C-15-17-18-G-F-20-D-C. In the recycling circuit I, the compressed homogeneous mixed phase is under homogeneous conditions. The recycling pump 17 conveys the mobile carrier phase consisting of CO.sub.2 and modifier through the extraction cell 19 and the static mixer 20 in the recycling circuit I, whereupon the lipophilic constituents (phospholipid and, where appropriate, cholesterol) previously introduced into the extraction cell 19 are dissolved. The UV detector 18 displays the degree of homogenisation of the compressed lipid-containing mixed phase with the lipophilic constituents introduced into the extraction cell 19. The detector signal is recorded on a plotter. The extraction cell 19 is a pressure-stable steel tube with threaded connectors and filters at the inlet and outlet. Emptied chromatographic columns may also be used for that purpose. The pressure sensor 21 measures the pressure downstream of the recycling circuit I. The pressure regulator 22 comprises a piezo crystal, which is controlled by the piezo driver 23 and thus establishes the required pressure conditions. The piezo driver 23 automatically establishes the required pressure independently of the flow conditions. In the arrangement 24a,b-30a,b-31a,b-32a,b water soluble or hydrophilic substance may be added to the system which are to be encapsulated in liposomes. The arrangement 24b-30b-31b-32b in the low pressure range is preferred. The addition in arrangement 24a-30a-31a-32a is also possible. The static mixer 25 serves as a homogeniser in the formation of liposomes. The recycling pump 27 conveys the aqueous phase from the collecting vessel 26 through the static mixer 33 into the recycling circuit II, which is defined by the arrangement 29-34-26-27-29. In that circuit, uncontrolled foam formation on depressurisation of the mixed phase is prevented and homogeneity of the depressurised mixed phase is established. The water bath 28 ensures that temperature conditions in the recycling circuit I, in the pump head of the

recycling pump 17 and in the detection cell 18 are constant. The three-way taps A,C,D,F,G,I,J,L,N allow the currents of the compressed phase to pass through (one outer always open) or distribute them in two directions (two outlets open). The two-way taps B,E,H,K,M,O allow the currents to flow through or prevent them from passing.

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